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## *Exhibit E*

### **PROSTATE SPECIFIC MEMBRANE ANTIGEN (PSMA) EXPRESSION IN NON-PROSTATE CANCERS**

JS Ross, K Gray, S Beddah, D Schenkein, I Webb, G Gray, N Leschly, R Mosher, R Meyer, J Deeds. Albany Medical College, Albany NY and Millennium Pharmaceuticals, Inc., Cambridge, MA

**Background:** PSMA, a transmembrane folate hydrolase, is expressed at low levels in normal prostate epithelium and is significantly overexpressed in prostate cancer (PCA) and the neovasculature of various non-PCAs. Non-PCA expression of PSMA is currently being pursued as a target for diagnostic imaging and anti-cancer antibody therapeutics.

**Design:** PSMA expression was measured on a series of fresh frozen non-PCA malignancies by transcriptional profiling (TP) using cDNA microarrays on nylon membranes, RT-PCR (Taqman), in situ hybridization, western blotting, dual co-localizatuion immunofluorescence (IF) and immunohistochemistry (IHC) both before and after laser capture microdissection (LCM).

**Results:** PSMA mRNA expression by ISH was localized to the neo-vasculature in 55% of a series of breast, colon, lung and ovarian cancers. PSMA mRNA expression measured by Taqman™ RT-PCR was localized to the endothelium of the tumor vessels after microdissection. Using IHC with the J-591 antibody to the external domain of PSMA on frozen sections, 40% of the same carcinomas were positive for PSMA immunoreactivity of the tumor vasculature. Dual IF studies using antibodies to PSMA and CD31 (PECAM-1) localized PSMA expression to the endothelium of neo-vasculature in carcinomas of the breast, colon, lung and ovary, in Wilm's tumors and neuroblastomas, but not in the tumor vessels of PCAs.

**Conclusion:** These molecular studies confirm that PSMA expression is highly associated with the neo-vasculature of many non-PCAs and co-localizes with endothelial cell markers. Further studies of PSMA in non-PCA as a target for both diagnostic imaging and anti-cancer antibody-based therapies appear warranted.

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